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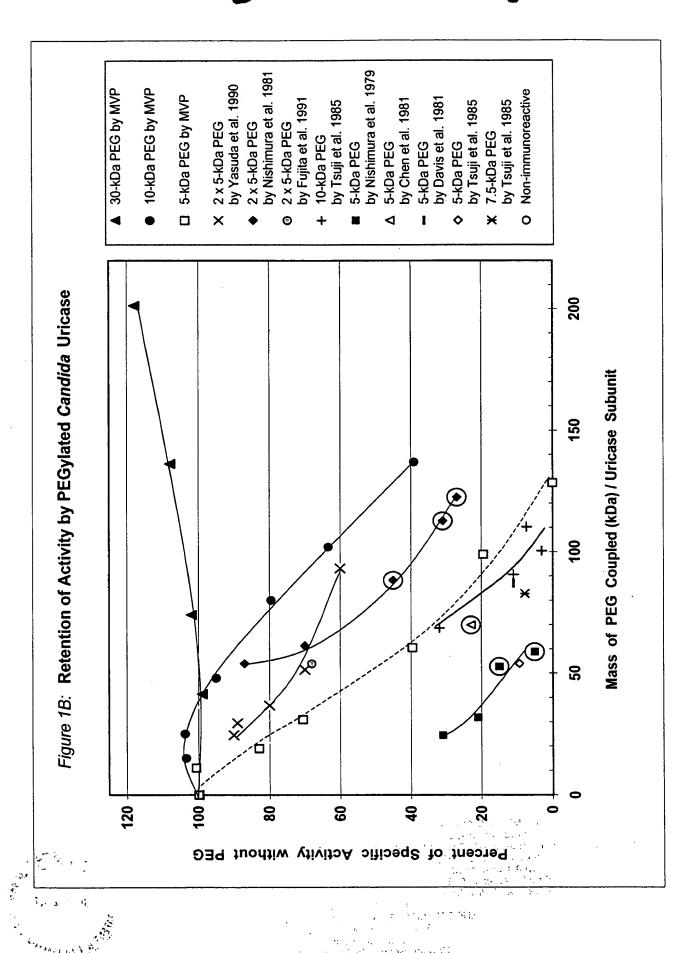
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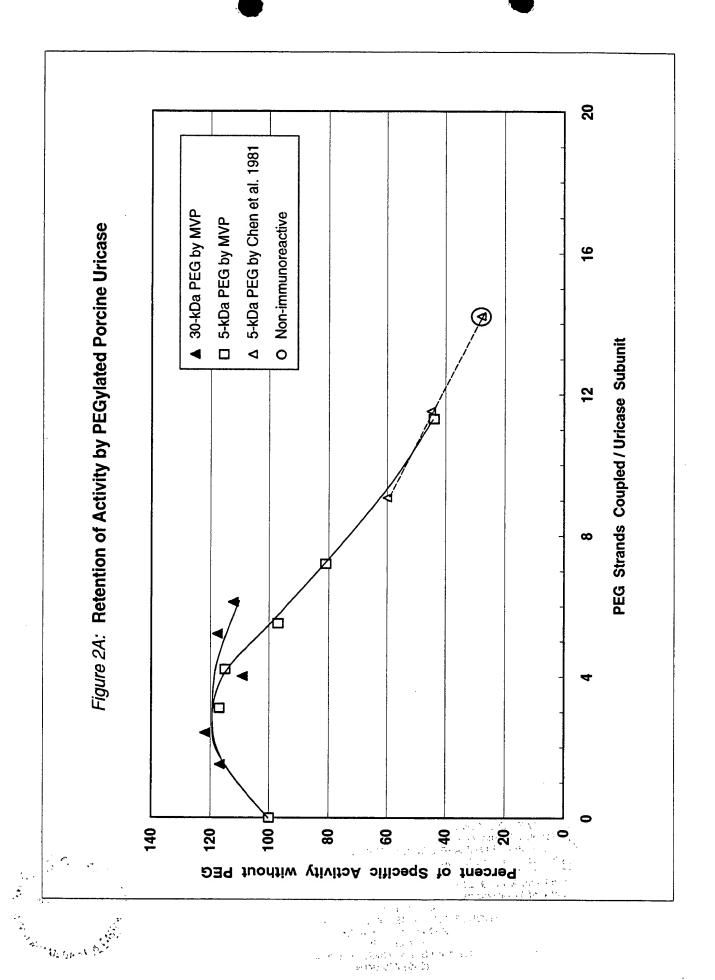
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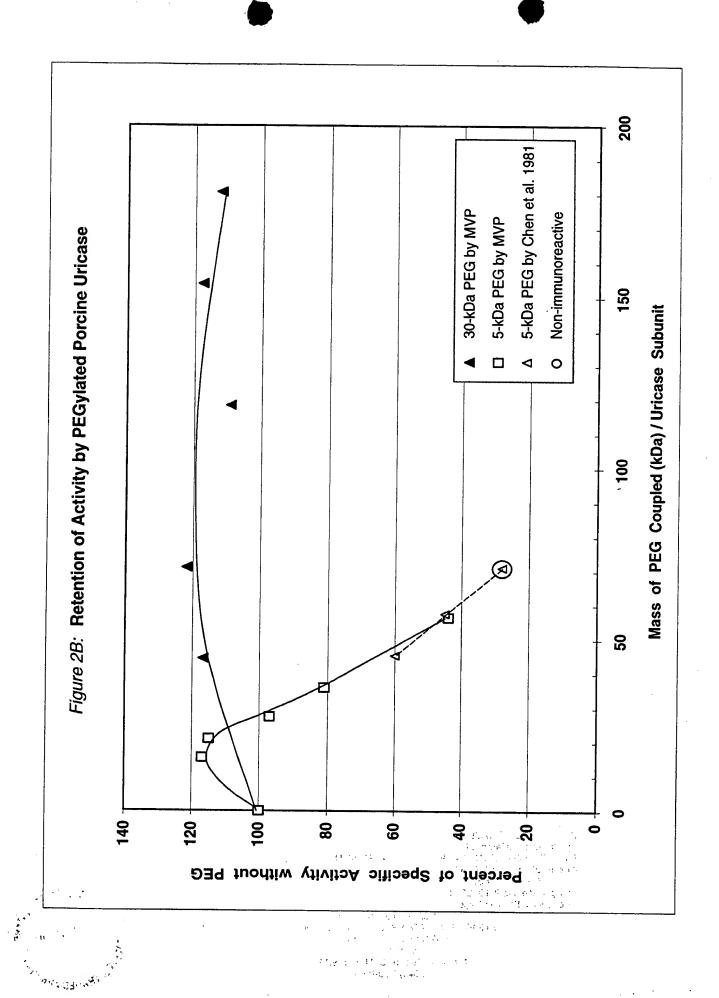
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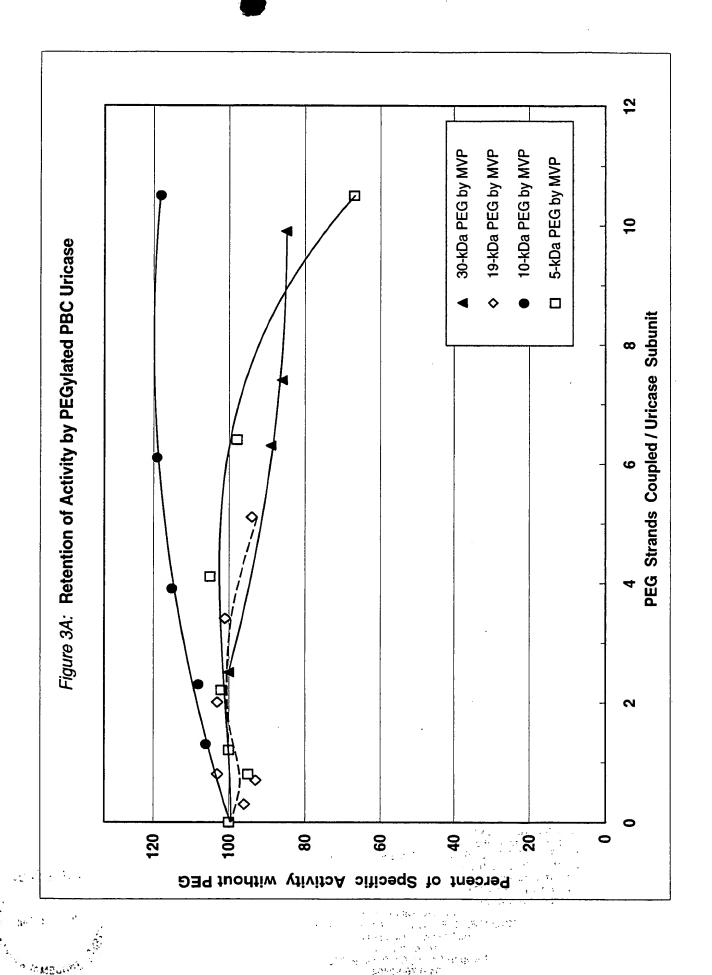
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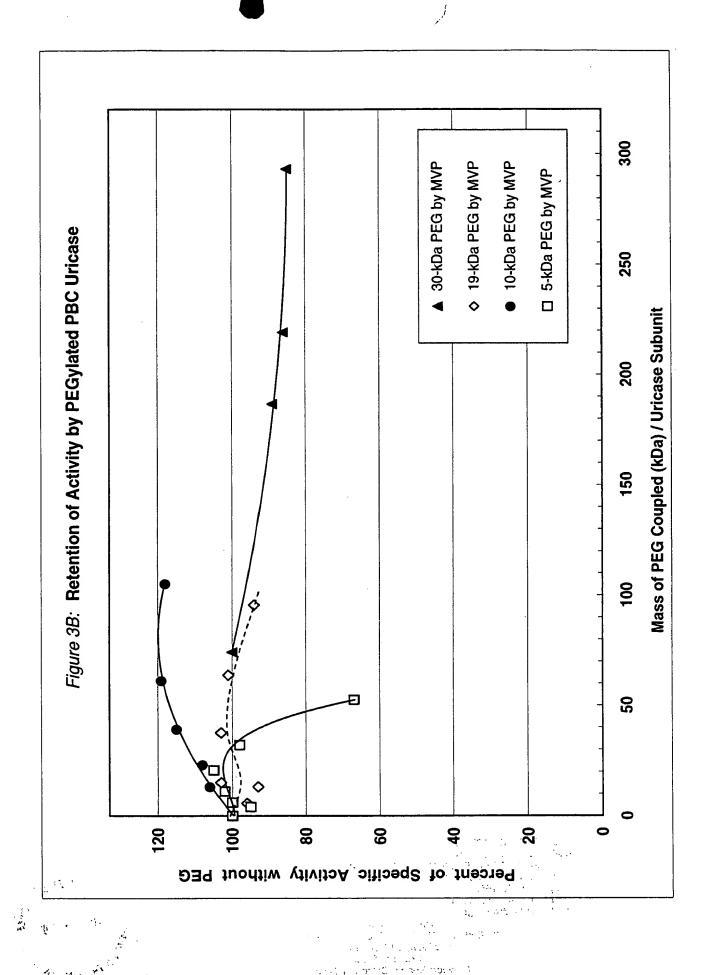
7.5 kDa PEG by Tsuji et al. 1985 by Nishimura et al. 1979 2 x 5-kDa PEG by Nishimura et al. 1981 by Yasuda et al. 1990 10-kDa PEG by MVP ▲ 30-kDa PEG by MVP Non-immunoreactive □ 5-kDa PEG by MVP 2 x 5-kDa PEG by Fujita et al. 1991 by Tsuji et al. 1985 by Davis et al. 1981 by Chen et al. 1981 by Tsuji et al. 1985 2 x 5-kDa PEG 10-kDa PEG 5-kDa PEG 5-kDa PEG 5-kDa PEG 5-kDa PEG × 0 × 0 **\rightarrow** ٥ Figure 1A: Retention of Activity by PEGylated Candida Uricase 25 PEG Strands Coupled / Uricase Subunit 20 19 100 内 8 9 6 20 Percent of Specific Activity without PEG

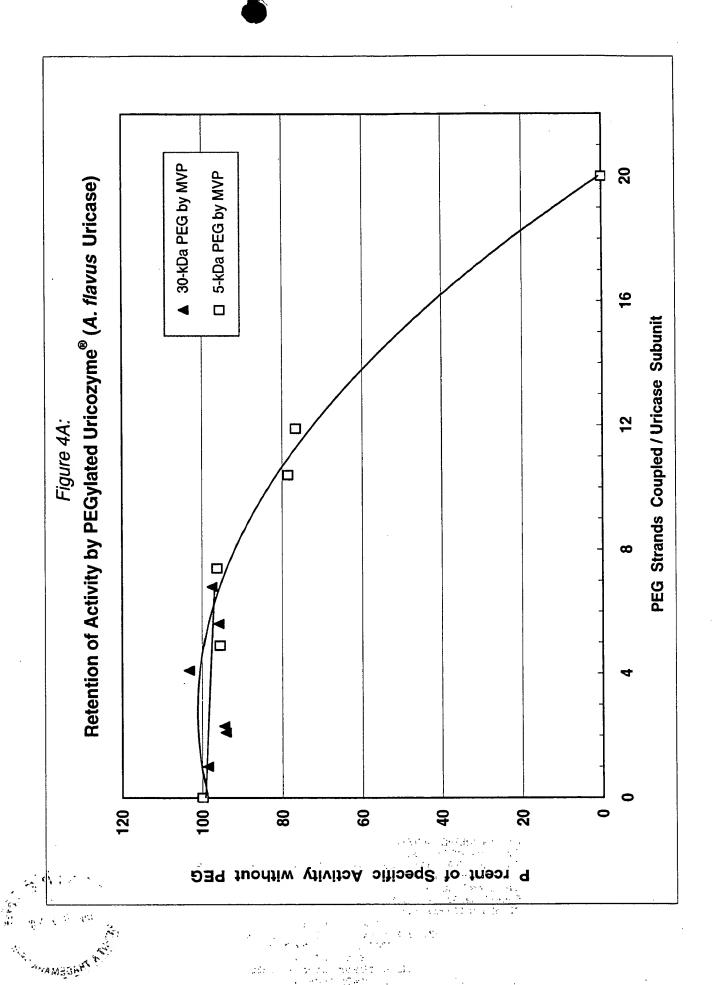


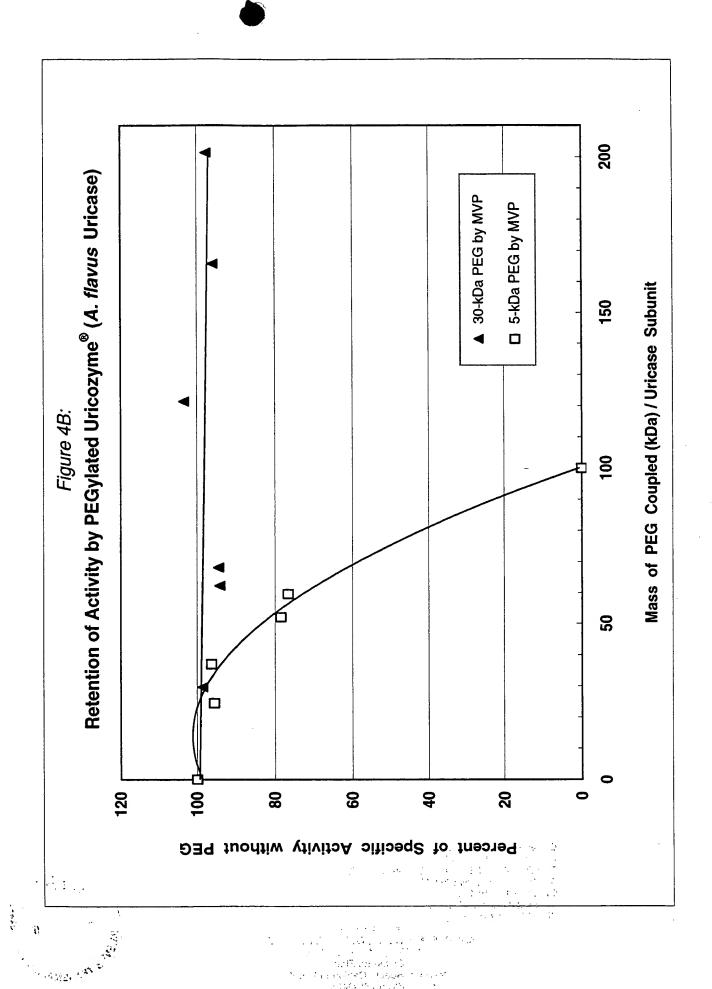


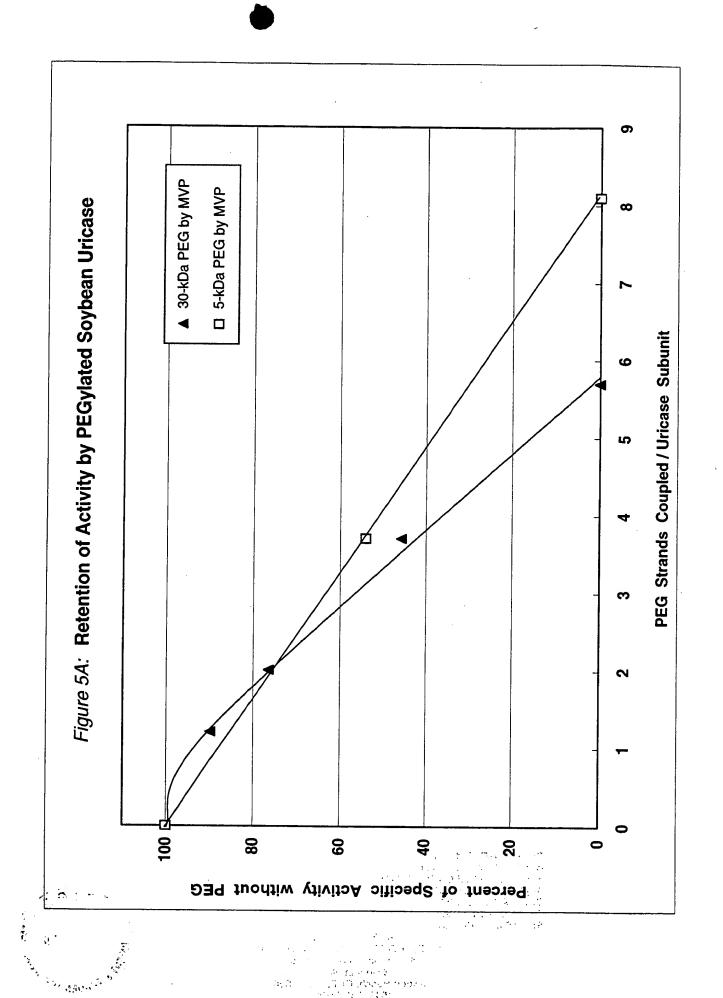












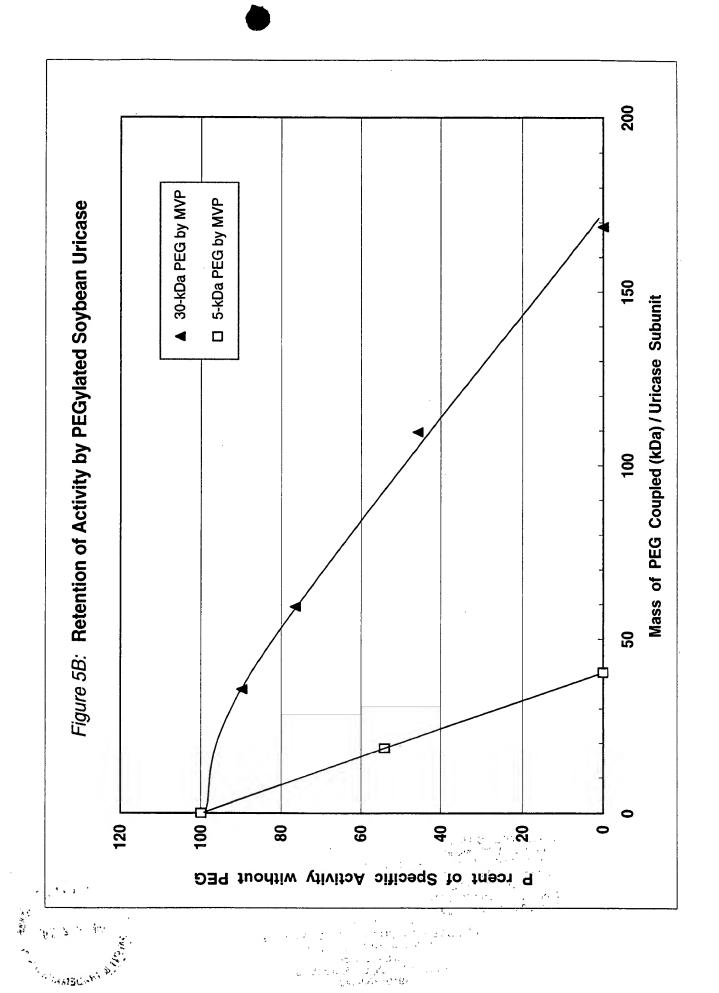
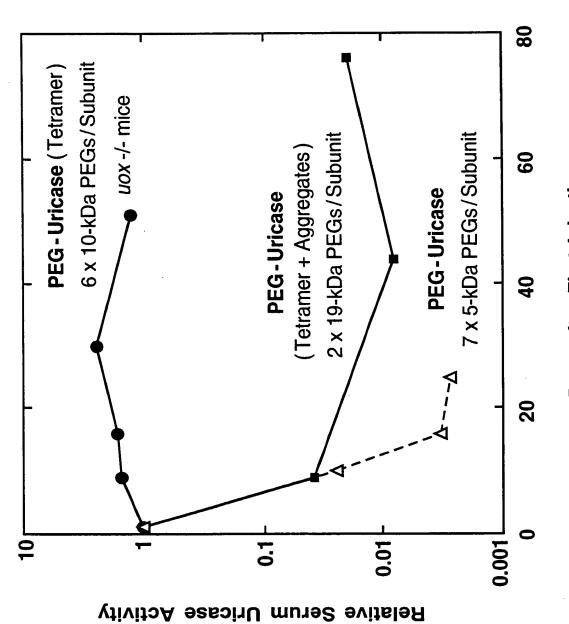


Figure 6: Deduced amino acid sequences of Pig-Baboon Chimeric (PBC) uricase, PBC uricase that is truncated at the amino and carboxyl terminals (PBC-NT-CT) and Porcine uricase containing the mutations R291K and T301S (PKS Uricase) (SEQ ID NO:3), compared with the porcine sequence (SEQ ID NO: 1) and baboon sequence (SEQ ID NO: 2)

•	Porcine	MAHYRNDYKK NDEVEFVRTG	YGKDMIKVLH IQRDGKYHSI	40
	PBC	porcine sequence 1-225		40
	PBC-NT-CT	porcine sequence		34
	PKS	porcine sequence 1-288		40
	Baboon	MADYHNNYKK NDELEFVRTG	YGKDMVKVLH IQRDGKYHSI	40
•	Porcine	KEVATSVOLT LSSKKDYLHG	DNSDVIPTDT IKNTVNVLAK	80
	PBC	porcine sequence →		80
	PBC-NT-CT	porcine sequence →		74
	PKS	porcine sequence →		80
	Baboon	KEVATSVQLT LSSKKDYLHG	DNSDIIPTDT IKNTVHVLAK	80
•	Porcine	FKGIKSIETF AVTICEHFLS	SFKHVIRAQV YVEEVPWKRF	120
	PBC	porcine sequence $\rightarrow$		120
	PBC-NT-CT	porcine sequence $\rightarrow$		114
	PKS	porcine sequence →		120
	Baboon	FKGIKSIEAF GVNICEYFLS	SFNHVIRAQV YVEEIPWKRL	120
	Porcine	EKNGVKHVHA FIYTPTGTHF	CEVEQIRNGP PVIHSGIKDL	160
	PBC	porcine sequence $ ightarrow$		160
	PBC-NT-CT	porcine sequence $ ightarrow$		154
	PKS	porcine sequence →		160
	Baboon	EKNGVKHVHA FIHTPTGTHF	CEVEQLRSGP PVIHSGIKDL	160
	Porcine	KVLKTTQSGF EGFIKDQFTT	LPEVKDRCFA TQVYCKWRYH	200
	PBC	porcine sequence $\rightarrow$		200
	PBC-NT-CT	porcine sequence →		194
	PKS	porcine sequence →		200
	Baboon	KVLKTTQSGF EGFIKDQFTT	LPEVKDRCFA TQVYCKWRYH	200
	Porcine	QGRDVDFEAT WDTVRSIVLQ	KFAGPYDKGE YSPSVQKTLY	240
	PBC	porcine sequence	$\rightarrow$ $\leftarrow$ baboon sequence	240
	PBC-NT-CT	porcine sequence	$\rightarrow$ $\leftarrow$ baboon sequence	234
	PKS	porcine sequence →		240
	Baboon	QCRDVDFEAT WGTIRDLVLE	KFAGPYDKGE YSPSVQKTLY	240
	Porcine	DIQVLTLGQV PEIEDMEISL	PNIHYLNIDM SKMGLINKEE	280
	PBC	baboon sequence $ ightarrow$		280
	PBC-NT-CT	baboon $sequence  ightarrow$		27 <u>4</u> 280
	PKS	porcine sequence →	DATINGATOM CVMCI TAIVEE	
	Baboon	DIQVLSLSRV PEIEDMEISL	PNIHYFNIDM SKMGLINKEE	280
	Porcine	VLLPLDNPYG RITGTVKRKL	TSRL 304 304	
	PBC	baboon sequence →	295	
	PBC-NT-CT	baboon sequence →		
	PKS	porcine ← baboon VLLPLDNPYG KITGTVKRKL	→ 304 SSRL 304	
	Baboon	VLLPLDNPYG KITGTVKRKL	SSRL 304	

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Figure 7: Serum Uricase Activity 24 Hours after Each PEG-Uricase Injection, Relative to the First Injection



Days after First Injection

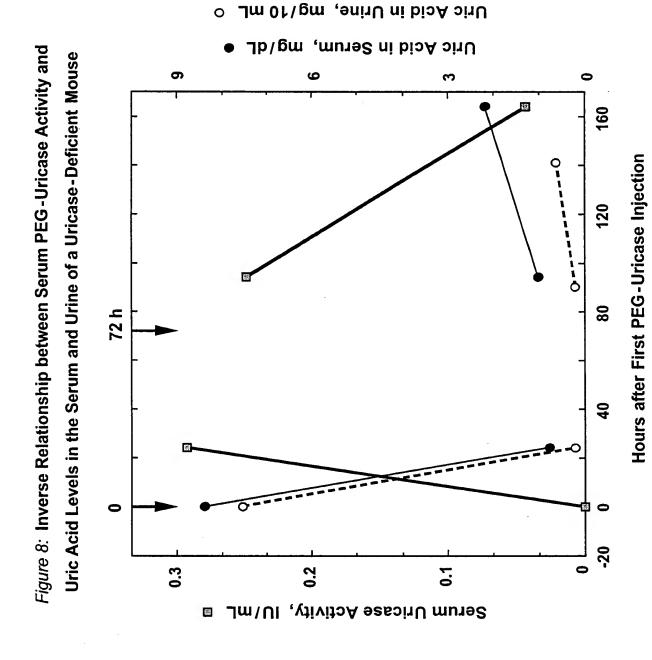
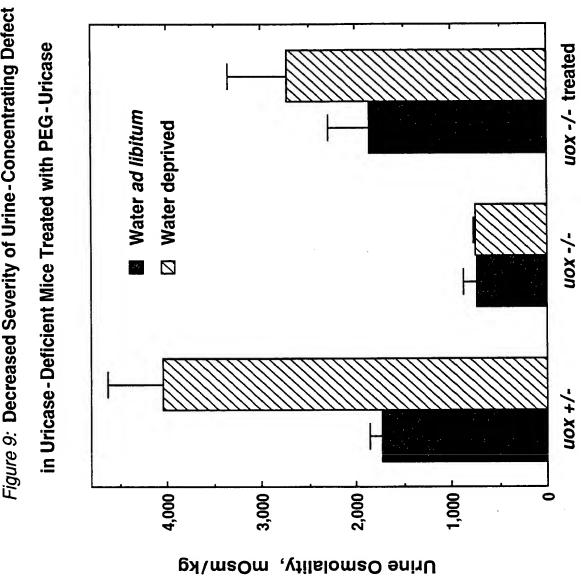


Figure 9: Decreased Severity of Urine-Concentrating Defect



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Figure 10: Decreased Severity of Nephrogenic Diabetes Insipidus in Uricase - Deficient Mice Treated with PEG-Uricase

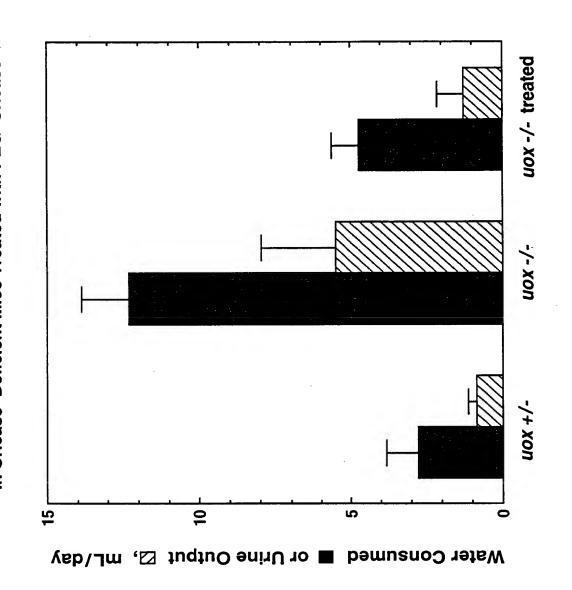
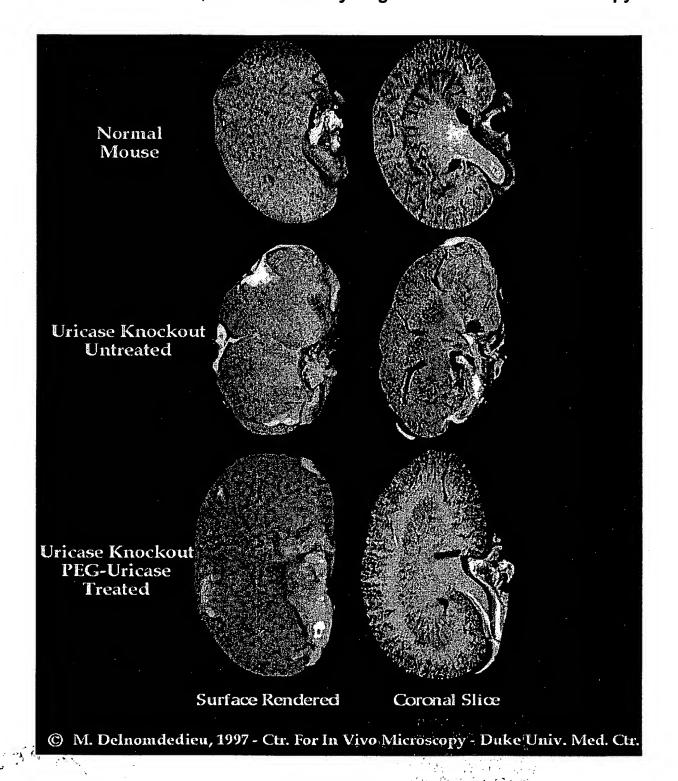


Figure 11:

Decreased S v rity of Uric Acid-Induced Nephropathy aft r Tr atment with PEG-Uricase, as Visualized by Magnetic Resonanc Microscopy



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Figure 12: Clearance from the Circulation of BALB/c Mice of PBC Uricase Tetramer and Octamer Coupled to 5-6 Strands of 10-kDa PEG/Subunit

